



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Srinivas G. Rao and Jay D. Kranzler

Serial No.: 10/628,141 Art Unit: 1614

Filed: July 24, 2003 Examiner: Not Yet Assigned

For: *TREATMENT AND PREVENTION OF DEPRESSION SECONDARY TO PAIN (DSP)*

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including six (6) pages of Form PTO-1449 and copies of the forty-nine (49) documents cited therein.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1868.

**U.S. Patents**

<u>Number</u>	<u>Issue Date</u>	<u>Patentee</u>	<u>Class/Subclass</u>
4,478,836	10-23-1984	Mouzin, et al.	424/248.54
4,535,186	08-13-1985	Husbands, et al.	564/336
4,761,501	08-12-1988	Husbands, et al.	564/167
4,939,175	07-03-1990	Ukai, et al.	514/646
4,956,388	09-11-1990	Robertson, et al.	514/651
5,621,142	04-15-1997	Mochizuki, et al.	564/164

U.S.S.N.: 10/628,141  
Filed: July 24, 2003

INFORMATION DISCLOSURE STATEMENT

**Foreign Documents**

<u>Number</u>	<u>Publication Date</u>	<u>Patentee</u>	<u>Country</u>
WO 95/22521	08-24-1995	Asahi Chemical Ind.	PCT

**Publications**

AKIL & LIEBESKIND, "Monoaminergic mechanisms of stimulation-produced analgesia," *Brain Res.* 94: 279-296 (1975).

BAKER & GREENSHAW, "Effects of long-term administration of antidepressants and neuroleptics on receptors in the central nervous system," *Cell Molec. Neurobiol.* 9(1): 1-44 (1989).

BECK, ed., Depression: Clinical, Experimental and Theoretical Aspects, Hoeber: New York (1967).

BERGE, et al., "Attenuation of morphine-induced analgesia by p-chlorophenylalanine and p-chloroamphetamine: test-dependent effects and evidence for brainstem 5-hydroxytryptamine involvement," *Brain Res.* 271: 51-64 (1983).

BLIER & DEMONTIGNY, "Current advances and trends in the treatment of depression," *Trends Pharmacol. Sci.* 15: 220-226 (1994).

BROWN, et al., "Depression: Distress or disease? Some epidemiological consideration," *Br. J. Psychiatry* 147: 612-622 (1985).

BUCKETT, et al., "The pharmacology of sibutramine hydrochloride (BTS 54 524), a new antidepressant which induces rapid noradrenergic down-regulation," *Prog. Nuero-Psychopharmacol. & Biol. Psychiatry* 12: 575-584 (1988).

DAVIDSON, et al., "Atypical depression," *Arch. Gen. Psychiatry* 39: 527-534 (1982).

DELGADO, et al., "Serotonin function and the mechanism of antidepressant action," *Arch. Gen. Psychiatry* 47: 411-418 (1990).

DEPREZ, et al., "Which bioequivalence study for a racemic drug? Application to milnacipran," *Eur. J. Drug Metab. Pharmacokinet.* 23(2): 166-171 (1998).

DOAN & WADDEN, "Relationships between depressive symptoms and descriptions of chronic pain," *Pain* 36: 75-84 (1989).

DOYLE & HU, "A new enantioselective synthesis of milnacipran and an analogue by catalytic asymmetric cyclopropanation," *Adv. Synth. Catal.* 343(3): 299-302 (2001).

U.S.S.N.: 10/628,141  
Filed: July 24, 2003  
INFORMATION DISCLOSURE STATEMENT

DWORKIN, et al., "Predicting treatment response in depressed and non-depressed chronic pain patients," *Pain* 24: 343-353 (1986).

FULLER & WONG, "Effects of antidepressants on uptake and receptor systems in the brain," *Prog Neuro-psychopharmacol. & Biol. Psychiatry* 9: 485-490 (1985).

HALEY, et al., "Depression in chronic pain patients: relation to pain, activity, and sex differences," *Pain* 23: 337-343 (1985).

JOYCE, et al., "Patterns and predictors of remission, response and recovery in major depression treated with fluoxetine or nortriptyline," *Australian & NZ J. Psychiatry* 36: 384-391 (2002).

KERNS & HAYTHORNTHWAITE, "Depression among chronic pain patients: cognitive-behavioral analysis and effect on rehabilitation outcome," *J. Consult. Clin. Psychol.* 56: 870-876 (1988).

KRISHNAN, et al., "Depression as a psychopathological disorder in chronic pain," in Chronic Pain (France, et al., eds.) American Psychiatric Press: Washington, DC, pp. 194-218 (1988).

KRISHNAN, et al., "Chronic pain and depression. II. Symptoms of anxiety in chronic low back pain patients and their relationship to subtypes of depression," *Pain* 22: 289-94 (1985).

MORET, et al., "Biochemical profile of midalcipran (F 2207), 1-phenyl-1-diethyl-aminocarbonyl-2-aminomethyl-cyclopropane (Z) hydrochloride, a potential fourth generation antidepressant drug," *Neuropharmacology* 24(12): 1211-1219 (1985).

OWENS & NEMEROFF, "Role of serotonin in the pathophysiology of depression: focus on the serotonin transporter," *Clin. Chem.* 40: 288-95 (1995).

PALMIER, et al., "Monoamine uptake inhibition by plasma from healthy volunteers after single oral doses of the antidepressant milnacipran," *Eur. J. Clin. Pharmacol.* 37(3): 235-238 (1989).

PAYKEL, et al., "Response to phenelzine and amitriptyline in subtypes of outpatient depression," *Arch. Gen. Psychiatry* 39: 1041-1049 (1982).

PAYKEL, et al., "Nosology of atypical depression," *Psychol. Med.* 13: 131-139 (1983).

PORTER, et al., "Single dose comparison of bicifadine, codeine and placebo in postoperative pain," *Curr. Therapeutic Res.* 30 (1981).

POST, et al., "Analgesia induced by 5-hydroxytryptamine receptor agonists is blocked or reversed by noradrenaline-depletion in rats," *Brain Res.* 363: 18-27 (1986).

U.S.S.N.: 10/628,141

Filed: July 24, 2003

INFORMATION DISCLOSURE STATEMENT

POTTER & MANJI, "Catecholamines in depression: an update," *Clin. Chem.* 40: 279-287 (1994).

QUITKIN, et al., "Phenelzine and imipramine in mood reactive depressives," *Arch. Gen. Psychiatry* 46: 787-93 (1989).

ROMANO & TURNER, "Chronic pain and depression: does the evidence support a relationship?" *Psychol. Bull.* 97: 18-34 (1985).

ROTHSCHILD, "Biology of depression," *Med. Clin. NA* 72: 765-90 (1988).

SHUTO, et al., "(+/-)-(Z)-2-(aminomethyl)-1-phenylcyclopropanecarboxamide derivatives as a new prototype of NMDA receptor antagonists," *J. Med. Chem.* 38: 2964-2968 (1995).

SHUTO, et al., "(1S,2R)-1-Phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide (PPDC), a new class of NMDA-receptor antagonist: molecular design by a novel conformational restriction strategy," *Jpn. J. Pharmacol.* 85: 207-213 (2001).

SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogs of milnacipran: (1S,2R)-1-phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide, an efficient noncompetitive N-methyl-D-aspartic acid receptor antagonist," *J. Med. Chem.* 39: 4844-4852 (1996).

SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogues of milnacipran: (1S,2R)-1-phenyl-2-[(R)-1-amino-2-propynyl]-N,N-diethylcyclopropanecarboxamide is a novel class of NMDA receptor channel blocker," *J. Med. Chem.* 41: 3507-3514 (1998).

SHUTO, et al., "Synthesis of (+)- and (-)-milnaciprins and their conformationally restricted analogs," *Tetrahedron Lett.* 37(5): 641-644 (1996).

SIMSON, et al., "Infusion of a monoamine oxidase inhibitor into the locus caeruleus can prevent stress-induced behavioral depression," *Biol. Psychiatry* 21: 724-34 (1986).

STEWART, et al., "Do age of onset and course of illness predict different treatment outcome among DSM IV depressive disorders with atypical features?" *Neuropsychopharmacol.* 26: 237-245 (2002).

STROLIN-BENEDETTI, "Biochimie de la dépression et des antidépresseurs," *Encephale*. 8(5): 545-585 (1982).

VETULANI & SULSER, "Action of various antidepressant treatments reduces reactivity of noradrenergic cyclic AMP-generating system in limbic forebrain," *Nature* 257: 495-496 (1975).

U.S.S.N.: 10/628,141

Filed: July 24, 2003

INFORMATION DISCLOSURE STATEMENT

VETULANI, et al., "A possible common mechanism of action of antidepressant treatments," *Naunyn-Schmiedeberg Arch Pharmacol* 293:109-114 (1976).

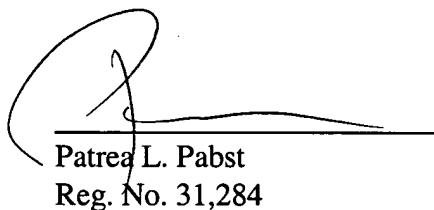
VIAZZO, et al., "Microbiological transformations 34: enantioselective hydrolysis of a key-lactone involved in the synthesis of the antidepressant milnacipran," *Tetrahedron Lett.* 37(26): 4519-4522 (1996).

WANG, et al., "The oral analgesic efficacy of bicifadine hydrochloride in postoperative pain," *J. Clin. Pharmacol.* 22: 160-164 (1982).

**Remarks**

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

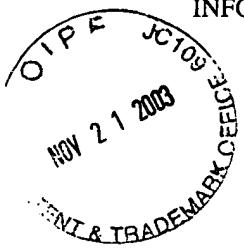


Patrea L. Pabst  
Reg. No. 31,284

Dated: November 19, 2003

HOLLAND & KNIGHT LLP  
One Atlantic Center  
1201 West Peachtree Street, N.E.  
Suite 2000  
Atlanta, Georgia 30309-3400  
404-817-8473  
FAX 404-817-8588  
[www.hklaw.com](http://www.hklaw.com)

U.S.S.N.: 10/628,141  
Filed: July 24, 2003  
INFORMATION DISCLOSURE STATEMENT



**Certificate of Mailing under 37 C.F.R. § 1.8(a)**

I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: November 19, 2003

Peggy Bailey

A handwritten signature of the name "Peggy Bailey" is written over a solid horizontal line. The signature is cursive and appears to be in black ink.

# 1363753\_v1

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-98)

**Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.**

Substitute for form 1449A/PTO		Complete if Known	
<p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p>(use as many sheets as necessary)</p>			
		<b>Application Number</b> 10/628,141 <b>Filing Date</b> July 24, 2003 <b>First Named Inventor</b> Srinivas G. Rao <b>Group Art Unit</b> 1614 <b>Examiner Name</b> <b>Attorney Docket Number</b> CYPR 101	
Sheet	1	of	6

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 6

**Complete if Known**

**Application Number** 10/628,141

**Filing Date** July 24, 2003

**First Named Inventor** Srinivas G. Rao

**Group Art Unit** **1614**

**Examiner Name**

Sheet 1 of 6 Attorney Docket Number

CYPR 101

U.S. PATENT DOCUMENTS

## FOREIGN PATENT DOCUMENTS

Examine Signature		Date Considered	
----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231.

L1 #1365132 v1

CYPR 101  
088938/00005

NOV 21 2003

Please type a plus sign (+) inside this box → 

PTO/SB/08A (10-08)

Approved for use through 10/31/99. OMB 0551-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**Complete if Known**

Application Number	10/628,141
Filing Date	July 24, 2003
First Named Inventor	Srinivas G. Rao
Group Art Unit	1614
Examiner Name	

Sheet 2 of 6 Attorney Docket Number CYPR 101

**OTHER ART -- NON PATENT LITERATURE DOCUMENTS**

Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		AKIL & LIEBESKIND, "Monoaminergic mechanisms of stimulation-produced analgesia," <i>Brain Res.</i> 94: 279-296 (1975).	
		BAKER & GREENSHAW, "Effects of long-term administration of antidepressants and neuroleptics on receptors in the central nervous system," <i>Cell Mol. Neurobiol.</i> 9(1): 1-44 (1989).	
		BECK, ed., <i>Depression: Clinical, Experimental and Theoretical Aspects</i> , Hoeber: New York (1967).	
		BERGE, et al., "Attenuation of morphine-induced analgesia by p-chlorophenylalanine and p-chloroamphetamine: test-dependent effects and evidence for brainstem 5-hydroxytryptamine involvement," <i>Brain Res.</i> 271: 51-64 (1983).	
		BLIER & DEMONTIGNY, "Current advances and trends in the treatment of depression," <i>Trends Pharmacol. Sci.</i> 15: 220-226 (1994).	
		BROWN, et al., "Depression: Distress or disease? Some epidemiological consideration," <i>Br. J. Psychiatry</i> 147: 612-622 (1985).	
		BUCKETT, et al., "The pharmacology of sibutramine hydrochloride (BTS 54 524), a new antidepressant which induces rapid noradrenergic down-regulation," <i>Prog. Nuero-Psychopharmacol. &amp; Biol. Psychiatry</i> 12: 575-584 (1988).	
		DAVIDSON, et al., "Atypical depression," <i>Arch. Gen. Psychiatry</i> 39: 527-534 (1982).	
		DELGADO, et al., "Serotonin function and the mechanism of antidepressant action," <i>Arch. Gen. Psychiatry</i> 47: 411-418 (1990).	
		DEPREZ, et al., "Which bioequivalence study for a racemic drug? Application to milnacipran," <i>Eur. J. Drug Metab. Pharmacokinet.</i> 23(2): 166-171 (1998).	

Examiner's Signature		Date Considered	
----------------------	--	-----------------	--

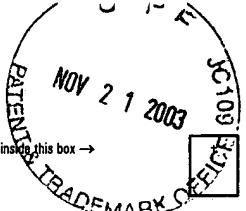
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>6</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>8</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+



Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98)  
Approved for use through 10/31/99. OMB 0651-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/628,141
Filing Date	July 24, 2003		
First Named Inventor	Srinivas G. Rao		
Group Art Unit	1614		
Examiner Name			
Sheet	3	of	6
		Attorney Docket Number	CYPR 101

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		DOAN & WADDEN, "Relationships between depressive symptoms and descriptions of chronic pain," <i>Pain</i> 36: 75-84 (1989).	
		DOYLE & HU, "A new enantioselective synthesis of milnacipran and an analogue by catalytic asymmetric cyclopropanation," <i>Adv. Synth. Catal.</i> 343(3): 299-302 (2001).	
		DWORKIN, et al., "Predicting treatment response in depressed and non-depressed chronic pain patients," <i>Pain</i> 24: 343-353 (1986).	
		FULLER & WONG, "Effects of antidepressants on uptake and receptor systems in the brain," <i>Prog Neuro-psychopharmacol. &amp; Biol. Psychiatry</i> 9: 485-490 (1985).	
		HALEY, et al., "Depression in chronic pain patients: relation to pain, activity, and sex differences," <i>Pain</i> 23: 337-343 (1985).	
		JOYCE, et al., "Patterns and predictors of remission, response and recovery in major depression treated with fluoxetine or nortriptyline," <i>Australian &amp; NZ J. Psychiatry</i> 36: 384-391 (2002).	
		KERNIS & HAYTHORNTHWAITE, "Depression among chronic pain patients: cognitive-behavioral analysis and effect on rehabilitation outcome," <i>J. Consult. Clin. Psychol.</i> 56: 870-876 (1988).	
		KRISHNAN, et al., "Depression as a psychopathological disorder in chronic pain," in <i>Chronic Pain</i> (France, et al., eds.) American Psychiatric Press: Washington, DC, pp. 194-218 (1988).	
		KRISHNAN, et al., "Chronic pain and depression. II. Symptoms of anxiety in chronic low back pain patients and their relationship to subtypes of depression," <i>Pain</i> 22: 289-94 (1985).	
		MORET, et al., "Biochemical profile of midalcipran (F 2207), 1-phenyl-1-diethyl-aminocarbonyl-2-aminomethyl-cyclopropane (Z) hydrochloride, a potential fourth generation antidepressant drug," <i>Neuropharmacology</i> 24(12): 1211-1219 (1985).	

Examiner's Signature	Date Considered
----------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-08)  
Approved for use through 10/31/99. OMB 0651-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/628,141
Filing Date	July 24, 2003		
First Named Inventor	Srinivas G. Rao		
Group Art Unit	1614		
Examiner Name			
Sheet	4	of	6
		Attorney Docket Number	CYPR 101

OTHER ART -- NON PATENT LITERATURE DOCUMENTS		
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published
		OWENS & NEMEROFF, "Role of serotonin in the pathophysiology of depression: focus on the serotonin transporter," <i>Clin. Chem.</i> 40: 288-95 (1995).
		PALMIER, et al., "Monoamine uptake inhibition by plasma from healthy volunteers after single oral doses of the antidepressant milnacipran," <i>Eur. J. Clin. Pharmacol.</i> 37(3): 235-238 (1989).
		PAYKEL, et al., "Response to phenelzine and amitriptyline in subtypes of outpatient depression," <i>Arch. Gen. Psychiatry</i> 39: 1041-1049 (1982).
		PAYKEL, et al., "Nosology of atypical depression," <i>Psychol. Med.</i> 13: 131-139 (1983).
		PORTER, et al., "Single dose comparison of bicifadine, codeine and placebo in postoperative pain," <i>Curr. Therapeutic Res.</i> 30 (1981).
		POST, et al., "Analgesia induced by 5-hydroxytryptamine receptor agonists is blocked or reversed by noradrenaline-depletion in rats," <i>Brain Res.</i> 363: 18-27 (1986).
		POTTER & MANJI, "Catecholamines in depression: an update," <i>Clin. Chem.</i> 40: 279-287 (1994).
		QUITKIN, et al., "Phenelzine and imipramine in mood reactive depressives," <i>Arch. Gen. Psychiatry</i> 46: 787-93 (1989).
		ROMANO & TURNER, "Chronic pain and depression: does the evidence support a relationship?" <i>Psychol. Bull.</i> 97: 18-34 (1985).
		ROTHSCHILD, "Biology of depression," <i>Med. Clin. NA</i> 72: 765-90 (1988).

Examiner's Signature	Date Considered
----------------------	-----------------

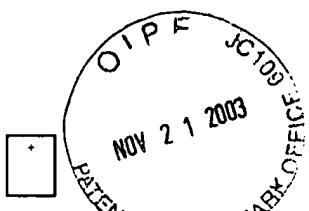
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-98)  
Approved for use through 10/31/99. OMB 0651-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			
Sheet	5	of	6
		Attorney Docket Number	
		CYPR 101	

#### OTHER ART -- NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		SHUTO, et al., "(+)-(-)-Z)-2-(aminomethyl)-1-phenylcyclopropanecarboxamide derivatives as a new prototype of NMDA receptor antagonists," <i>J. Med. Chem.</i> 38: 2964-2968 (1995).	
		SHUTO, et al., "(1S,2R)-1-Phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide (PPDC), a new class of NMDA-receptor antagonist: molecular design by a novel conformational restriction strategy," <i>Jpn. J. Pharmacol.</i> 85: 207-213 (2001).	
		SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogs of milnacipran: (1S,2R)-1-phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide, an efficient noncompetitive N-methyl-D-aspartic acid receptor antagonist," <i>J. Med. Chem.</i> 39: 4844-4852 (1996).	
		SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogues of milnacipran: (1S, 2R)-1-phenyl-2-[(R)-1-amino-2-propynyl]-N,N-diethylcyclopropanecarboxamide is a novel class of NMDA receptor channel blocker," <i>J. Med. Chem.</i> 41: 3507-3514 (1998).	
		SHUTO, et al., "Synthesis of (+)- and (-)-milnaciprane and their conformationally restricted analogs," <i>Tetrahedron Lett.</i> 37(5): 641-644 (1996).	
		SIMSON, et al., "Infusion of a monoamine oxidase inhibitor into the locus caeruleus can prevent stress-induced behavioral depression," <i>Biol. Psychiatry</i> 21: 724-34 (1986).	
		STEWART, et al., "Do age of onset and course of illness predict different treatment outcome among DSM IV depressive disorders with atypical features?" <i>Neuropsychopharmacol.</i> 26: 237-245 (2002).	
		STROLIN-BENEDETTI, "Biochimie de la dépression et des antidépresseurs," <i>Encephale</i> 8(5): 545-585 (1982).	
		VETULANI & SULSER, "Action of various antidepressant treatments reduces reactivity of noradrenergic cyclic AMP-generating system in limbic forebrain," <i>Nature</i> 257: 495-496 (1975).	
		VETULANI, et al., "A possible common mechanism of action of antidepressant treatments," <i>Naunyn-Schmiedeberg Arch Pharmacol</i> 293:109-114 (1976).	

Examiner's Signature	Date Considered
----------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

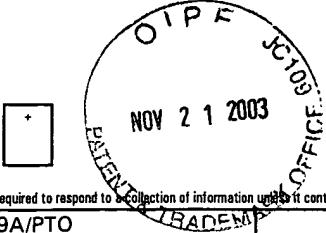
<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-88)

**Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.**

**Substitute for form 1449A/PTO**

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Substitute for form 1449A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		Application Number	10/628,141
(use as many sheets as necessary)		Filing Date	July 24, 2003
		First Named Inventor	Srinivas G. Rao
		Group Art Unit	1614
		Examiner Name	
Sheet	6	of	6
		Attorney Docket Number	CYPR 101

## OTHER ART -- NON PATENT LITERATURE DOCUMENTS

Examiner's Signature		Date Considered	
-------------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.